



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Legal aspects on (proactive) transparency of clinical data - EMA perspective

University Basel, Faculty of Law – 16 December 2016

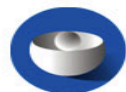
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Overview



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Publication of clinical reports

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02/10/2014

Publication of clinical reports

EMA adopts landmark policy to take effect on 1 January 2015

The European Medicines Agency (EMA) has decided to publish the clinical reports that underpin the decision-making on medicines. Following extensive consultations held by the Agency with patients, healthcare professionals, academia, industry and other European entities over the past 18 months, the EMA Management Board unanimously adopted the new policy at its meeting on 2 October 2014. The policy will enter into force on 1 January 2015. It will apply to clinical reports contained in all applications for centralised marketing authorisations submitted after that date. The reports will be released as soon as a decision on the application has been taken.

"The adoption of this policy sets a new standard for transparency in public health and pharmaceutical research and development," said Guido Rasi, EMA Executive Director. "This unprecedented level of access to clinical reports will benefit patients, healthcare professionals, academia and industry."

The new EMA policy will serve as a useful complementary tool ahead of the implementation of the new EU Clinical Trials Regulation that will come into force not before May 2016. EMA expects the new policy to increase trust in its regulatory work as it will allow the general public to better understand the Agency's decision-making. In addition, academics and researchers will be able to re-assess data sets. The publication of clinical reports will also help to avoid duplication of clinical trials, foster innovation

Related documents

- [European Medicines Agency policy on publication of clinical data for medicinal products for human use \(02/10/2014\)](#)
- [Questions and answers on the European Medicines Agency policy on publication of clinical data for medicinal products for human use \(03/10/2014\)](#)

Related content

- [Release of data from clinical trials](#)
- [Publication and access to clinical-trial data: an inclusive development process](#)

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Policy 0070 on proactive publication of clinical data

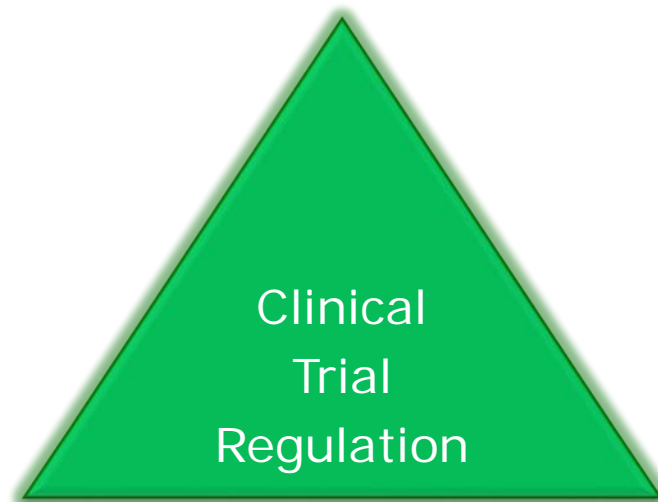
- **Date of coming into effect of policy** – 1 January 2015
- **Stepwise implementation:**
 - First phase: publication of clinical reports commenced in **October 2016**
 - Applies to any new MAAs and Article 58 applications, submitted after **1 January 2015**
 - Applies to modification of indication or line extension applications for existing CAPs, submitted after **1 July 2015**
 - Applies to all other post-authorisation applications for existing CAPs submitted – date to be determined
 - Second phase: review of various aspects on individual patient data (IPD) will follow
- **Scope:**
 - Clinical data: clinical reports (i.e. clinical overviews (module 2.5), clinical summaries (module 2.7) and clinical study reports - CSRs (module 5), together with appendices 16.1.1, 16.1.2 and 16.1.9)
 - Submitted under the centralised procedure



Clinical data publication policy and Clinical Trial Regulation (1/2)



Clinical data publication policy:
all the clinical reports (trials located in
EU or outside EU) in the regulatory
submission to EMA



Clinical Trial Regulation:
EU clinical trials



Clinical data publication policy and Clinical Trial Regulation (2/2)

	Clinical data publication policy (Policy 0070)	Clinical Trial Regulation (Regulation (EU) No 536/2014)
Medicinal products covered	Centrally authorised products only	Investigational medicinal products regardless of whether they have a marketing authorisation
Clinical studies covered	Clinical studies submitted to the Agency in the context of a MAA, Article 58 procedure, line extension or new indication, regardless of where the study was conducted	Clinical trials conducted in the EU and paediatric trials conducted outside the EU that are part of paediatric investigation plans
Documents published	Clinical data (clinical overview, clinical summaries and clinical study reports) and the anonymisation report	All clinical trial-related information generated during the life cycle of a clinical trial (e.g. protocol, assessment and decision on trial conduct, summary of trial results including a lay summary, study reports, inspections, etc.)
Publication channel	EMA clinical data publication website	Future EU portal and database
Date it applies	1 January 2015 (MAA or Article 58 procedure) or 1 July 2015 (line extension or new indication)	Expected October 2018
Publication from	October 2016	Expected in 2019



EMA Policy on clinical data publication: The final deliverable

- **Achieving a balanced approach addressing competing interests:** need to allow access to clinical data and discourage unfair commercial use of the data, through the introduction of a publication process, based on 2 pillars:
 - Terms of use (ToU) governing the access to and use of clinical reports;
 - User-friendly tool allowing access to the clinical reports.
- **Two sets of ToU depending on the user's needs:**
 - Clinical reports, available on-screen, for any user;
 - For general information purposes;
 - Simple and limited registration process.
 - Clinical reports, downloadable, available to identified users:
 - For academic and non-commercial research purposes;
 - Registration process includes the need to provide elements concerning the identity of the user.



EMA policy on clinical data publication: The final deliverable

- **Common elements to both sets of ToU:**
 - Trial subjects may not be re-identified;
 - Clinical reports may not be used to support a MAA/post-authorisation procedure, and no unfair commercial use may be made;
 - Watermark is applied to the published information;
 - EMA accepts no responsibility for compliance with the ToU.



Clinical Data Publication (Policy 0070) - External Guidance

Introduction, scope, definitions

Guidance on the procedural aspects related to the submission of clinical reports for the purpose of publication in accordance with EMA policy 0070

Guidance on the identification and redaction of commercially confidential information (CCI) in clinical reports submitted to the EMA

Guidance to pharmaceutical industry on the anonymisation of clinical reports for the purpose of publication in accordance with EMA policy 0070

Published on EMA website: **3 March 2016**



Guidance on the identification and redaction of CCI in clinical reports for publication

- As a matter of principle, only in limited circumstances clinical reports may contain CCI and could be subject to redaction.
- Annex 3 to the EMA policy identifies certain types of information that potentially may be considered CCI.
- Proposals for redaction need to be justified and will be reviewed by EMA who will take the final decision
- Guidance on what EMA would not consider CCI:
 - Information that is already in the public domain or publically available;
 - Information that does not bear any innovative features;
 - Additional information the disclosure of which would be in the public interest;
 - Any information lacking sufficient or relevant justification.



Guidance on the anonymisation of clinical reports for publication (1/2)

- Marketing authorisation holders (MAHs)/applicants have the responsibility for submitting clinical reports that have been rendered anonymous for the purpose and use of such clinical reports (publication under EMA policy).
- EU data protection legislation needs to be complied with by EMA and by the MAH/applicant:
Data in the clinical reports must be processed in such a way that it can no longer be used to identify a natural person by using "*all means likely reasonably to be used*" (Directive 95/46/EC).
- Article 29 Data Protection Working Party Opinion on anonymisation techniques has been the basis of the guidance developed. Several available standards have also been taken into account.
- The information contained in the guidance is not binding and should be considered EMA recommendations to MAHs/applicants on how to best achieve anonymisation.



Guidance on the anonymisation of clinical reports for publication (2/2)

- Anonymisation techniques:
 - Several techniques are available to MAHs/applicants (legislation is not prescriptive);
 - Is a field of active research and rapidly evolving.
- EMA guidance recommends to MAHs/applicants how to best achieve anonymisation:
 - EMA favours anonymisation techniques that will optimise the clinical usefulness (data utility) of the information published;
 - EMA understands that in an initial phase MAHs/applicants are likely to use masking (due to the need for retrospective anonymisation of the data) which may decrease the clinical utility of the data in an initial phase.
- EDPS has been consulted on the EMA draft guidance on anonymisation.
- The setting-up of a technical anonymisation group (TAG) is foreseen for 2017 to establish best practice.



Overview



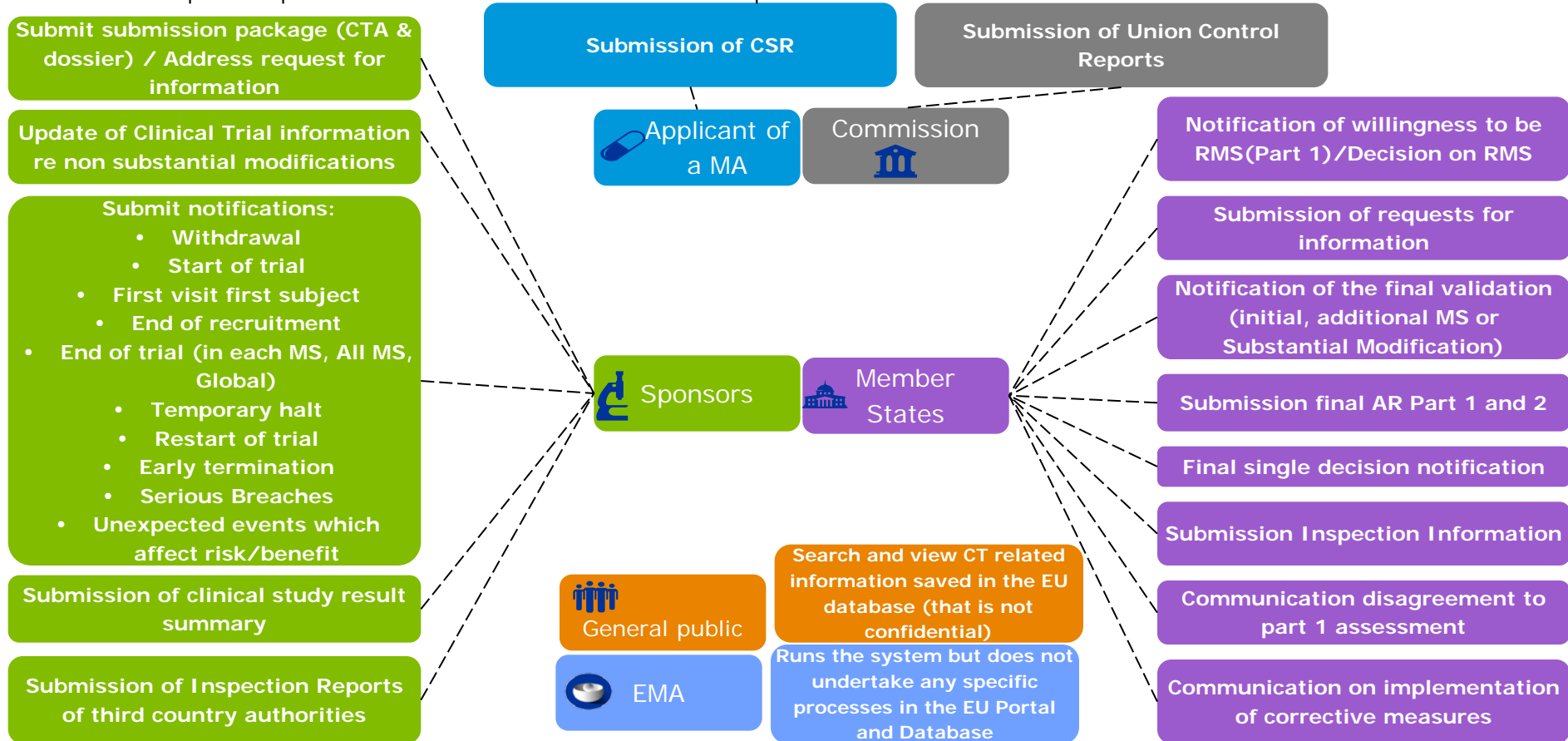


Scope of Clinical Trial Regulation (EU) No 536/2014

- Interventional clinical trials on medicinal products conducted in the EU/EEA (i.e. with at least one investigator site in EU/EEA).
- Clinical trials authorised under the new Regulation or still ongoing three years after it comes into application.

Processes for each stakeholders in the system

This slide depicts the processes each stakeholder will be able to complete in the new EU Portal and Database:



Transparency legal requirements: Clinical Trial Regulation

Article 81(4) of Regulation (EU) No 536/2014

- EU database shall be publically accessible by default, with exceptions justified on any of the following grounds:
 - Protection of personal data;
 - Protection of commercially confidential information, in particular taking into account the MA status of the medicinal product, unless there is an overriding public interest in disclosure;
 - Protecting confidential communication between Member States in relation to the preparation of the assessment report;
 - Ensuring effective supervision of the conduct of a clinical trial by Member States.

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EMA/228363/2015 Endorsed

Appendix, on disclosure rules, to the “Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014”

Draft reviewed with the clinical trials information system expert group	8 December 2014
Consultation with the MS for release for public consultation	9 December 2014 - 13 January 2015
Consultation with the European Commission for release for public consultation	9 December 2014 - 13 January 2015
Public consultation	21 January - 18 February 2015
Consultation of the final document by the European Commission	7 September 2015
Consultation of the final document by the Member States	7 September 2015
Endorsement by European Medicines Agency Management Board	2 October 2015
Sign off by the Deputy Executive Director	5 October 2015

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- Appendix, on disclosure rules, to the “Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014”
- Endorsed on 2 October 2015 by EMA Management Board and published on 6 October 2015

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/10/WC500195084.pdf



Objectives of rules on public disclosure

- Have all clinical trials been publicly registered?
- Is there a trial in which I could participate?
- What was the outcome of the trial I participated in?
- What trials were the basis of the marketing authorisation, what were their results?
- What is known about the medicine I am taking/prescribing?
- Can we review the data used to support the marketing authorisation?
- Has the trial we are designing already been conducted? Were there problems with similar trials?
- Strike the right balance to inform the public, protect public health and foster the innovation capacity of European medical research.



Functional specifications of EU portal and database

- **Single EU portal and database to support:**
 - One application dossier for each clinical trial or modification to it;
 - Coordinated approach to clinical trial authorisation and supervision;
 - Transparency of clinical trial authorisation, conduct and results.
- **Strike the right balance between:**
 - respecting patients' and doctors' needs and the public's entitlement to extensive and timely information about clinical trials;
 - developers' and researchers' need to protect their investments;
 - a balanced approach is needed to protect public health and also foster the innovation capacity of European medical research.



Requirements for operation of a feasible system

- To enable public access to the database, rules for the application of the exceptions, set out in Article 81(4), are required.
- Rules, criteria and data to enable the system software to determine, automatically, when a particular data element or document should be made public.
- Automatic rules are necessary because there will be 4-5,000 clinical trial applications, dozens of documents and hundreds of data fields per clinical trial and multiple processes per trial taking place in the system every year.
- Rules designed to produce a consistent and predictable outcome so that those submitting data and documents and those viewing them know what will be made public and when.
- A manual override available to enable earlier publication in exceptional circumstances where an overriding public interest applies, or to remediate a publication error.



Summary of rules

- The same rules apply whether the sponsor is a pharmaceutical company, academic research group or other type of organisation.
- The rules depend on the IMPs used in a trial and how they are used.
- Trials defined as belonging to one of three categories, at the time of initial assessment of the clinical trial application:
 - **Category One:** Pharmaceutical development trials– essentially Phase I trials in healthy or patient (adult) volunteers, bio-equivalence and biosimilarity trials;
 - **Category Two:** Therapeutic exploratory and confirmatory trials - essentially Phase II and III trials of novel products or new indications or formulations of existing products;
 - **Category Three:** Therapeutic use trials – essentially Phase IV and low-intervention trials.
- Depending on the category of trial the sponsor will have the possibility to defer publication of certain data and documents up to a maximum time limit, if needed, to protect commercially confidential information.
- The use of deferrals will be monitored and should not exceed what is really needed.



Summary of Rules

- The default is to make documents and data public at the first opportunity.
- All data and documents in the system will be made public except for manufacturing/quality information, details of financial agreements between sponsors and investigators, and specified personal data.
- Public registration of trials at their start including all information needed for patients who may wish to participate in trials with therapeutic, diagnostic or preventive objectives.
- Publication of all results (summary, layperson summary and in case of MAA the clinical study report).
- Possibility of justified deferral for summary results only in case of category I trials up to a maximum of 30 months post end of trial (i.e. maximum 18 months deferral).
- Option to defer publication of the IMP Dossier, Investigator's Brochure, protocol and subject information sheet, up to maximum of: 7 years post end of trial for category I and 5 years for category II or the time of MA using that trial, whichever is earlier.



Protecting personal data

- EU database shall contain personal data only insofar as this is necessary (Article 81(6)).
- Clinical trial subjects evaluated for or participating in a trial:
 - No personal data of trial subjects shall be included in the database (Recital 67).
- Clinical trial investigator information to be made public:
 - Principal Investigators' names, name and addresses of clinical trial sites;
 - Principal Investigators' CVs containing only professional information relevant to the clinical trial (template to be provided);
 - Economic interests, institutional affiliations that might influence impartiality (template to be provided);
 - Name of Head of clinic/institution, or responsible person issuing written statement testifying to suitability of facilities.



Summary - Clinical Trial Transparency – and EMA

- **Clinical Trials authorised in EU/EEA:**
 - Growing body of clinical trial information and results summaries in EU Clinical Trial Register for trials authorised since 2004.
 - Clinical Trial Regulation - Extensive information on clinical trials from authorisation to the trial summary results of all trials authorised in EU/EEA under the new Regulation.
- **Clinical Study Reports submitted in Marketing Applications in EU:**
 - All clinical study reports included in marketing applications to the EMA from 1 January 2015
 - Clinical study reports for all trials authorised in EU/EEA under the Clinical Trial Regulation and included in a marketing application in EU.



Thank you for your attention

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